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Simultaneous Binding of Two Different Transition Metals to the DNA Model Base 1-Methylthymine: the X-Ray Structure of Bis[bis(μ-1-methylthyminato-N3,O4)-*cis*-diammine platinum(II)] Silver Nitrate Pentahydrate

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Two heteronuclear complexes of 1-methylthymine with cis-*Pt*$(NH_3)_2^{2+}$ *and* Ag^+ *binding to N(3) and O(4), respectively, have been prepared. The structure of one of these compounds,* $Ag[$cis-$Pt(NH_3)_2(C_6H_7N_2O_2)_2]_2NO_3\cdot 5H_2O$*, has been determined by X-ray diffraction and refined to* R = *0.048 for 4971 reflections. The compound crystallizes in the triclinic space group* $P\bar{1}$ *and has cell dimensions* a = *14.122(11),* b = *13.422(23),* c = *11.747(12) Å,* α = *101.60(10),* β = *100.01(8),* γ = *95.94(11)°* *with two formula units in the unit cell. The molecular cation consists of two bis(1-methylthyminato-N3)-*cis*-diammineplatinum(II) units connected by a silver cation* via *the exocyclic C(4) oxygen atoms. An explanation for the unexpected ligand properties of N(3) platinated 1-methylthymine is proposed.*

Introduction

It is well established now that the binding of platinum(II) antitumor agents to DNA is related to their activity [1]. With regard to the site(s) of DNA interaction(s), no definite conclusions have been reached as yet. Although there is some evidence that binding of *cis*-Pt$(NH_3)_2^{2+}$ to guanine may be of importance [2], recent findings on the synergistic effect of different platinum drugs [3] indicate that different modes of platinum–DNA interactions may exist.

As part of a program aimed at the systematic synthesis of reaction products between *cis*-diammineplatinum(II) residues and the four major bases of DNA and their investigation by X-ray analysis and spectroscopic techniques [4, 5] we have isolated bis(1-methylthyminato-N3)*cis*-diammineplatinum(II) as a model compound for a hypothetical 1:2-platinum–thymidine interaction. When studying the complex forming properties of this compound, we recently found that, with additional "*cis*-Pt$(NH_3)_2$-$(H_2O)_2^{2+}$" [6], a dimeric platinum complex with head-to-head arranged 1-methylthyminato ligands is formed [7]. We herewith report the preparation of two novel heteronuclear complexes of 1-methylthymine with platinum and silver as metal centers, bis(μ-1-methylthyminato)*cis*-diammine platinum(II)-silver nitrate tetrahydrate and bis[bis(μ-1-methylthyminato)*cis*-diammineplatinum(II)]-silver nitrate pentahydrate, and the X-ray structure of the latter.

Experimental Section

Preparation

Cis-$Pt(NH_3)_2Cl_2$ (Degussa) was reacted with slightly less than the stoichiometric amount of $AgNO_3$ to prepare *cis*-$[Pt(NH_3)_2(H_2O)_2](NO_3)_2$ [6]. Four equivalents of 1-methylthymine and two equivalents NaOH were added and the resulting mixture (0.06 *M* based on Pt) was kept in a stoppered flask for two days at 65 °C. Then the solution was heated to 95 °C and filtered from a small amount of a colorless precipitate, identified as *trans*-$[Pt(NH_3)_2$-$(C_6H_7N_2O_2)_2]\cdot H_2O$ by alternative preparation from *trans*-$Pt(NH_3)_2Cl_2$/1-methylthymine/NaOH, by IR-spectroscopy and elemental analysis [8].

The resulting solution was brought to pH ~ 6 (1 *N* HNO_3), concentrated to a small volume by rotary evaporation, cooled, filtered from unreacted 1-methylthymine (slightly more than two equivalents), and the resulting solution allowed to evaporate at room temperature. After 2–3 days colorless columns of bis(1-methylthyminato)*cis*-diammineplatinum(II) were collected. Yield 20% based on Pt. The crystals are rapidly loosing water of crystallization and transparency when kept on air. A sample with partial loss of water analyzes as 2.5 hydrate: *Anal.* Found: C 26.12, H 4.71, N 15.24%. Calcd. for $C_{12}H_{25}N_6O_{6.5}Pt$: C 26.08, H 4.57, N 15.21%. Recrystallization from methanol at room tempera-

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ture yields the monohydrate as colorless crystals: *Anal.* Found: C 27.09, H 4.21, N 16.04, Pt 37.0%. Calcd: C 27.43, H 4.23, N 15.99, Pt 37.13%.

From the aqueous solution obtained after filtration of *cis*-$[Pt(NH_3)_2(C_6H_7N_2O_2)_2]\cdot 2.5H_2O$, several other products have been isolated which are under investigation.

Bis[bis(μ-1-methylthyminato)*cis*-diammineplatinum(II)]-silver nitrate pentahydrate, $[Pt(NH_3)_2C_6H_7N_2O_2)_2]_2AgNO_3\cdot 5H_2O$, was obtained by addition of ¼ of the stoichiometric amount of $AgNO_3$ to an aqueous solution of *cis*-$[Pt(NH_3)_2(C_6H_7N_2O_2)_2]$ aq (*e.g.* 280 mg, 21 mg $AgNO_3$, 15 ml H_2O) and allowing the solution to evaporate slowly at room temperature. Within two days a few bright transparent crystals had formed. After 10 days 120 mg of the title compound were collected and briefly dried on air. The crystals are very sensitive when kept on air: within 2–3 minutes they burst with loss of water of crystallization. Elemental analyses were performed immediately after isolation from solution. Results would be in slightly better agreement with the compound formulated as a hexahydrate, but this may be due to incomplete drying of the crystals: *Anal.* Found: C 22.05, H 4.13, N 14.09, Ag 8.0%. Calcd. for $C_{24}H_{50}N_{13}O_{16}AgPt_2$ (pentahydrate): C 22.61, H 3.96, N 14.29, Ag 8.46%.

Addition of more than ¼ of Ag per Pt, *e.g.* ½, does not result in a better yield of the title compound but in partial formation of the Pt/Ag = 1:1 complex besides the title compound.

Bis(μ-1-methylthyminato)*cis*-diammineplatinum(II)-silver nitrate tetrahydrate, $Pt(NH_3)_2C_6H_7N_2O_2)_2AgNO_3\cdot 4H_2O$, was obtained in a similar way as the Pt/Ag = 2:1 product when 1 equivalent of $AgNO_3$ per Pt was added. The product precipitated rapidly and was recrystallized from hot water. Colorless transparent microplates. Yield 65%. *Anal.* Found: C 19.52, H 3.68, N 12.59, Ag 14.2%. Calcd. for $C_{12}H_{28}N_7O_{11}Ag$ Pt: C 19.23, H 3.77, N 13.09, Ag 14.39%.

Infrared Spectra

IR spectra were recorded on a Perkin Elmer 580 grating spectrometer as KBr discs and Nujol mulls.

Crystallography

A crystal of the Pt/Ag = 2:1 complex (dimensions approximately 0.3 X 0.4 X 0.3 mm) was sealed in a capillary together with a drop of water to prevent bursting of the crystal. The cell parameters and the space group were determined at room temperature on a Syntex $P2_1$ diffractometer: a = 14.122(11), b = 13.422(23), c = 11.747(12) Å, α = 101.60(10), β = 100.01(8), γ = 95.94(11)°, V = 2125.7 Å^3, $P\bar{1}$, Z = 2, μ = 74.3 cm^{-1}, $d_{\text{calcd.}}$ = 1.99 gcm^{-3}, d_{measd} = 1.99 gcm^{-3} (flotation in CH_3I/CCl_4), Mo-K_α, λ = 0.71069 Å, graphite monochromator. 6486 reflections were measured ($2° \leqslant 2\theta \leqslant 50.0°$) and Lorentz, polarization and absorption corrections were applied. The structure was solved by direct methods with MULTAN (SYNTEX-XTL system). Full matrix least-squares refinement with anisotropic thermal parameters for the heavy and all oxygen and nitrogen atoms gave a final R value of 0.048 (4971 independent reflections with $F_{obs} > 4.5\sigma_{F_{obs}}$). Atomic positional and thermal parameters for the nonhydrogen atoms are listed in Table I.

Results and Discussion

Description of the Structure

The molecular cation of bis[bis(μ-1-methylthyminato-N3, O4)*cis*-diammineplatinum(II)] silver nitrate pentahydrate is shown in Fig. 1. Interatomic distances and angles around Pt and Ag are listed in Table II. The numbering scheme of atoms is as indicated in Fig. 2.

The cation is built up of two bis(1-methylthyminato-N3)*cis*-diammineplatinum(II) units which are arranged in such a way that the oxygen atoms of the exocyclic C(4)O groups are creating a cavity with the silver cation in it. Each platinum(II) has its usual square planar coordination with two ammine groups and two N(3) atoms of the thyminato ligands in *cis*-positions. The Pt–NH_3 distances differ slightly but are close to values previously observed in *cis*-diammineplatinum(II) complexes [5, 6]. The bond lengths between the two platinum atoms and the N(3) donor atoms of the 1-methylthymine ligands do not differ significantly and are within the range found in related

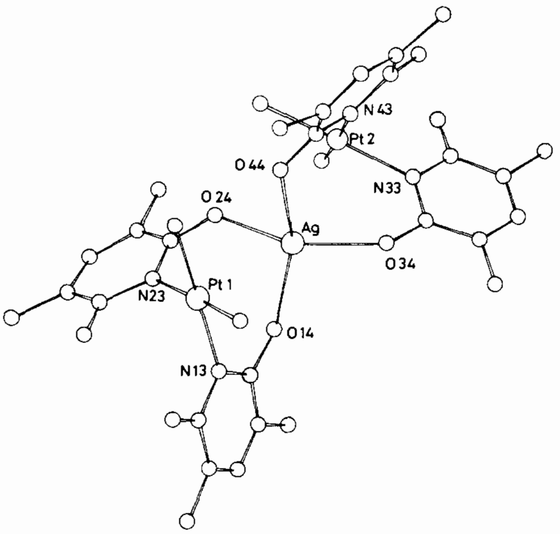

Fig. 1. The molecular cation $[cis\text{-}(NH_3)_2Pt(C_6H_7N_2O_2)_2]_2Ag^+$. The two Pt atoms and Ag are put in the drawing plane.

TABLE I. Atomic Coordinates and Thermal Parameters for the non-Hydrogen Atoms. The Anisotropic Temperature Factor is of the form: $T = \exp - \frac{1}{4} (b_{11}h^2a^{*2} + \ldots\ldots + 2b_{12}hka^*b^* + \ldots\ldots)$; b_{ij} in $Å^2$. Standard Deviation in Parentheses.

Atom	x/a	y/b	z/c	B
Pt(1)	−0.06743(4)	−0.14568(4)	−0.17949(5)	
Ag	−0.2297(1)	−0.2090(1)	−0.3722(1)	
Pt(2)	−0.40440(4)	−0.35387(4)	−0.47099(5)	
N(1)	−0.110(1)	−0.003(1)	−0.129(1)	
N(13)	0.015(1)	−0.087(1)	−0.282(1)	
O(14)	−0.079(1)	−0.184(1)	−0.453(1)	
C(14)	0.000(1)	−0.124(1)	−0.402(1)	2.8(3)
C(15)	0.066(1)	−0.093(1)	−0.469(1)	2.7(3)
C(151)	0.052(1)	−0.142(1)	−0.598(1)	
C(16)	0.142(1)	−0.021(1)	−0.414(1)	2.9(3)
N(11)	0.156(1)	0.019(1)	−0.297(1)	
C(11)	0.241(1)	0.104(1)	−0.233(2)	4.8(4)
C(12)	0.094(1)	−0.013(1)	−0.226(1)	2.8(3)
O(12)	0.107(1)	0.024(1)	−0.120(1)	
N(23)	−0.021(1)	−0.285(1)	−0.225(1)	
C(22)	0.070(1)	−0.293(1)	−0.163(1)	3.3(3)
O(22)	0.117(1)	−0.217(1)	−0.087(1)	
N(21)	0.108(1)	−0.383(1)	−0.190(1)	
C(21)	0.206(1)	−0.396(1)	−0.130(1)	4.0(3)
C(26)	0.052(1)	−0.465(1)	−0.282(1)	3.5(3)
C(25)	−0.038(1)	−0.458(1)	−0.331(1)	2.8(3)
C(251)	−0.101(2)	−0.546(1)	−0.419(2)	
C(24)	−0.077(1)	−0.369(1)	−0.302(1)	3.1(3)
O(24)	−0.163(1)	−0.364(1)	−0.349(1)	
N(2)	−0.151(1)	−0.205(1)	−0.074(1)	
N(33)	−0.438(1)	−0.262(1)	−0.588(1)	
C(34)	−0.408(1)	−0.160(1)	−0.562(1)	2.4(3)
C(35)	−0.446(1)	−0.097(1)	−0.631(1)	2.9(3)
C(351)	−0.417(1)	0.018(1)	−0.598(2)	
O(34)	−0.344(1)	−0.121(1)	−0.466(1)	
C(36)	−0.507(1)	−0.144 (1)	−0.734(1)	3.2(3)
N(31)	−0.531(1)	−0.249(1)	−0.769(1)	
C(31)	−0.597(1)	−0.303(1)	−0.882(2)	4.8(4)
C(32)	−0.497(1)	−0.311(1)	−0.696(1)	3.7(3)
O(32)	−0.518(1)	−0.404(1)	−0.723(1)	
N(43)	−0.479(1)	−0.278(1)	−0.355(1)	
C(44)	−0.429(1)	−0.222(1)	−0.243(1)	3.5(3)
O(44)	−0.339(1)	−0.214(1)	−0.221(1)	
C(45)	−0.484(1)	−0.181(1)	−0.168(1)	2.8(3)
C(451)	−0.431(1)	−0.131(2)	−0.041(1)	
C(46)	−0.580(1)	−0.189(1)	−0.194(1)	3.1(3)
N(41)	−0.629(1)	−0.239(1)	−0.303(1)	
C(41)	−0.740(1)	−0.246(1)	−0.344(1)	4.2(4)
C(42)	−0.580(1)	−0.289(1)	−0.391(1)	3.0(3)
O(42)	−0.624(1)	−0.343(1)	−0.487(1)	
N(3)	−0.366(1)	−0.444(1)	−0.357(1)	
N(4)	−0.332(1)	−0.439(1)	−0.588(1)	
O(1)	−0.285(1)	0.052(1)	−0.276(1)	
O(2)	−0.167(1)	−0.334(1)	−0.649(1)	
O(3)	−0.297(1)	0.103(1)	−0.021(1)	
O(4)	−0.273(1)	0.243(1)	−0.349(1)	
O(5)	0.473(3)	0.564(3)	0.871(3)	8.3(8)
O(6)	0.046(3)	0.765(3)	0.121(4)	10.6(11)
N(51)	0.294(3)	0.374(3)	0.946(4)	7.5(10)
O(51)	0.202(3)	0.345(3)	0.891(3)	8.8(9)
O(52)	0.351(3)	0.363(3)	0.892(4)	11.4(12)

(continued overleaf)

TABLE I. *(continued)*

Atom	x/a	y/b	z/c	B
O(53)	0.327(3)	0.407(3)	1.050(4)	11.5(12)
N(61)	0.124(5)	0.500(5)	0.098(6)	11.8(18)
O(61)	0.079(3)	0.444(4)	0.038(4)	10.5(12)
O(62)	0.120(3)	0.627(3)	0.164(3)	10.3(11)
O(63)	0.191(4)	0.535(4)	0.154(4)	11.8(14)

Atom	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
Pt(1)	2.28(3)	2.69(3)	2.21(2)	0.17(2)	0.40(2)	0.65(2)
Ag	2.65(5)	3.44(5)	3.63(5)	0.17(4)	−0.15(4)	0.99(4)
Pt(2)	2.60(3)	2.29(3)	3.01(3)	0.19(2)	0.48(2)	0.69(2)
N(1)	5.1(8)	3.2(6)	3.0(6)	1.8(6)	1.8(6)	1.0(5)
N(13)	2.6(6)	2.5(5)	2.0(5)	0.6(5)	−0.1(4)	0.6(4)
O(14)	3.7(6)	5.2(6)	2.6(5)	−0.4(5)	0.3(4)	0.0(4)
C(151)	4.7(9)	6.2(10)	2.3(7)	1.8(8)	1.5(7)	0.8(7)
N(11)	2.8(6)	3.9(7)	3.3(6)	0.2(5)	0.6(5)	1.2(5)
O(12)	3.7(5)	4.6(6)	2.4(4)	−1.0(5)	0.6(4)	0.6(4)
N(23)	2.6(6)	3.1(6)	1.8(5)	0.3(5)	0.2(4)	1.0(4)
O(22)	3.6(6)	4.4(6)	4.2(6)	0.5(5)	−0.5(5)	0.3(5)
N(21)	3.2(7)	4.3(7)	4.5(7)	0.8(6)	0.6(6)	1.4(6)
C(251)	5.9(11)	2.8(8)	7.3(12)	−0.7(8)	0.2(10)	−0.9(8)
O(24)	2.6(5)	2.7(5)	6.1(6)	−0.1(4)	−0.7(5)	1.3(4)
N(2)	3.6(6)	4.0(6)	1.1(4)	−0.4(5)	−0.1(5)	1.0(4)
N(33)	2.7(6)	3.3(6)	1.3(4)	0.1(5)	0.6(4)	0.2(4)
C(351)	4.9(10)	3.1(8)	5.3(9)	1.0(7)	1.1(8)	1.7(7)
O(34)	3.3(5)	2.5(5)	4.1(5)	0.2(4)	−0.6(4)	0.8(4)
N(31)	3.3(7)	5.4(8)	2.7(6)	0.4(6)	−0.1(5)	1.6(5)
O(32)	6.0(7)	3.8(6)	3.4(5)	−1.1(5)	0.6(5)	−0.3(4)
N(43)	2.1(6)	2.6(6)	3.6(6)	0.2(5)	0.6(5)	0.6(4)
O(44)	2.6(5)	7.0(7)	3.0(5)	0.6(5)	0.2(4)	0.3(5)
C(451)	4.7(10)	6.9(11)	2.4(7)	−0.2(9)	0.9(7)	−0.3(7)
N(41)	3.7(7)	3.8(7)	4.6(7)	1.8(6)	1.4(6)	2.2(5)
O(42)	2.4(5)	3.5(5)	3.7(5)	0.1(4)	−0.3(4)	0.0(4)
N(3)	3.0(6)	3.5(6)	3.7(6)	−0.2(5)	−0.2(5)	1.3(5)
N(4)	3.9(7)	2.4(6)	6.6(8)	1.3(5)	1.8(7)	0.0(6)
O(1)	5.8(7)	5.2(7)	4.9(6)	1.8(6)	−1.4(6)	0.7(5)
O(2)	8.2(10)	6.1(8)	5.6(7)	−0.7(7)	2.2(7)	−1.2(6)
O(3)	4.4(7)	6.5(8)	9.0(9)	−0.2(6)	1.9(7)	−0.3(7)
O(4)	7.1(9)	7.4(9)	7.1(8)	1.4(7)	2.2(7)	2.8(7)

TABLE II. Interatomic Distances (A) and Angles (deg) of the Metal Atoms.[a]

Distances			
Pt(1)–N(1)	2.069(13)	Pt(2)–N(3)	2.023(13)
Pt(1)–N(2)	2.057(12)	Pt(2)–N(4)	2.087(15)
Pt(1)–N(13)	2.022(11)	Pt(2)–N(33)	2.056(11)
Pt(1)–N(23)	2.046(12)	Pt(2)–N(43)	2.043(12)
Pt(1)–Ag	2.849(1)	Pt(2)–Ag	2.884(1)
Ag–O(14)	2.482(12)	Pt(1)–Pt(2)	5.469(1)
Ag–O(24)	2.412(14)	Pt(1)–Pt(1^{+})	5.073(1)
Ag–O(34)	2.353(11)	Pt(2)–Pt(2^{+})	4.386(1)
Ag–O(44)	2.563(11)		

(continued on facing page)

TABLE II. *(continued)*

Angles			
N(1)–Pt(1)–N(13)	89.5(5)	N(3)–Pt(2)–N(4)	87.8(5)
N(1)–Pt(1)–N(23)	178.0(5)	N(3)–Pt(2)–N(33)	178.0(5)
N(1)–Pt(1)–N(2)	90.6(5)	N(3)–Pt(2)–N(43)	90.0(5)
O(14)–Ag–O(24)	79.2(4)	Pt(1)–Ag–Pt(2)	145.11(5)
O(24)–Ag–O(34)	152.1(4)		
O(34)–Ag–O(44)	86.3(4)		
O(44)–Ag–O(14)	159.6(4)		

[a] $Pt(1^+)$ is related to Pt(1) by operation –x, –y, –z; $Pt(2^+)$ is related to Pt(2) by operation –1 – x, –1 – y, –1 – x;

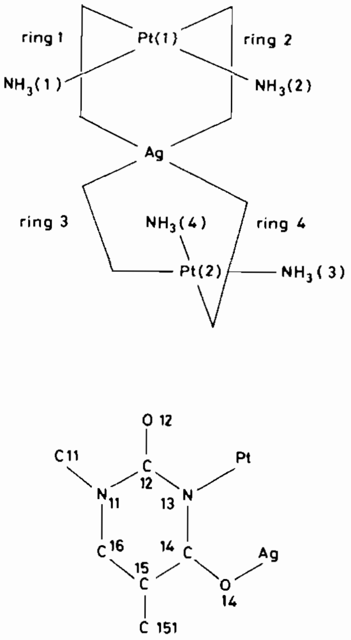

Fig. 2. Schematic drawing of the molecular cation and numbering scheme of atoms. Rings, 2, 3, 4 are numbered analogously, *e.g.* C(22) instead of C(12), N(23) instead of N(13) *etc.*

platinum–1-methylthymine complexes [7, 9]. The environments around both platinums are closely planar with deviations of the platinum atoms from the best planes being ±0.01 Å for Pt(1) and ±0.03 Å for Pt(2). The angles of the heterocyclic ligand planes with the platinum coordination planes are 64.0° and 77.9° for Pt(1) and 116.9° and 114.8° for Pt(2).

The tilting occurs for two adjacent 1-methylthymine ligands each in the same direction. This is not unexpected, since any tilting of two *cis*-standing 1-methylthymine ligands towards each other would lead to a repulsion between the lone pair electrons of the exocyclic oxygens of adjacent rings. The observed deviations from perpendicular positions of the ligand planes relative to the Pt coordination planes appears to be caused by the binding of Ag to the O(4) atoms. With binding of a second platinum to the exocyclic oxygens, the rings are forced to take positions approximately perpendicular to the platinum coordination planes as a consequence of the square planar coordination of platinum(II) [7].

The coordination around silver is distorted tetrahedral with oxygens of the exocyclic oxygen atoms of four 1-methylthymine ligands as closest neighbours. There is a possible ambiguity with respect to the donor atoms of Ag. If N(1) and C(5) in each 1-methylthymine ligand are interchanged, binding to Ag could also occur *via* O(2) instead of O(4). However, for reasons discussed before [9] and confirmed in this study, coordination of silver appears to be through O(4) [10]. Metal coordination through O(4) and N(3) has been observed in the head-to-tail dimer bis(μ-1-methylthyminato-N3,O4)bis-(*cis*-diammineplatinum(II))dinitrate [9] and, though less certain for one of the two ligands, in the corresponding head-to-head dimer [7]. For the respective head-to-tail dimer with 1-methyluracil instead of 1-methylthymine as bridging ligands, N(3), O(4) coordination has been confirmed unambiguously [11]. It therefore appears safe to assume that O(4) is the most basic site in N(1) substituted pyrimidine-2.4 diones once the N(3) position is platinated.

The environment of silver is shown in Fig. 3. Distances between Ag and its oxygen donors do differ considerably. Thus the Ag–O distance with ring 3 (Ag–O(34) = 2.353(11) Å) is shorter than are the Ag–O distances with the other three rings (2.412(12), 2.482(12) and 2.563(12) Å). The observed Ag–O(34) distance is close to that found in a dimeric 1-methylcytosine complex with Ag binding to N(3) and O(2) (2.367(2) Å) [12], and slightly shorter than those in silver compounds with essentially ionic bonding, *e.g.* $AgNO_3$ [13, 14], $AgNO_3$•alkene [14] or $AgNO_2$ [15] with distances of 2.45 Å and more. Ag–O interactions in our compound are, however, clearly weaker than in compounds with nitrogen

TABLE III. Interatomic Distances (Å) and Bond Angles (deg) within 1-Methylthymine Ligands.

Distances			
N(13)–C(14)	1.363(18)	N(23)–C(24)	1.370(20)
C(14)–O(14)	1.285(19)	C(24)–O(24)	1.246(20)
C(14)–C(15)	1.413(22)	C(24)–C(25)	1.379(22)
C(15)–C(151)	1.500(21)	C(25)–C(251)	1.496(25)
C(15)–C(16)	1.339(21)	C(25)–C(26)	1.324(23)
C(16)–N(11)	1.343(19)	C(26)–N(21)	1.425(21)
N(11)–C(11)	1.542(23)	N(21)–C(21)	1.488(23)
N(11)–C(12)	1.399(20)	N(21)–C(22)	1.379(22)
C(12)–O(12)	1.222(1)	C(22)–O(22)	1.247(20)
C(12)–N(13)	1.385(19)	C(22)–N(23)	1.390(20)
N(33)–C(34)	1.343(19)	N(43)–C(44)	1.402(20)
C(34)–O(34)	1.296(17)	C(44)–O(44)	1.238(21)
C(34)–C(35)	1.369(21)	C(44)–C(45)	1.349(23)
C(35)–C(351)	1.513(23)	C(45)–C(451)	1.529(22)
C(35)–C(36)	1.343(21)	C(45)–C(46)	1.328(23)
C(36)–N(31)	1.383(22)	C(46)–N(41)	1.348(20)
N(31)–C(31)	1.482(23)	N(41)–C(41)	1.548(23)
N(31)–C(32)	1.366(22)	N(41)–C(42)	1.436(21)
C(32)–O(32)	1.219(21)	C(42)–O(42)	1.233(18)
C(32)–N(33)	1.380(20)	C(42)–N(43)	1.385(21)
Angles			
C(12)–N(13)–C(14)	119.5(12)	C(22)–N(23)–C(24)	121.0(13)
Pt(1)–N(13)–C(12)	118.1(9)	Pt(1)–N(23)–C(22)	115.1(10)
Pt(1)–N(13)–C(14)	122.2(10)	Pt(1)–N(23)–C(24)	123.5(10)
N(13)–C(14)–C(15)	121.2(13)	N(23)–C(24)–C(25)	119.1(14)
O(14)–C(14)–C(15)	120.6(14)	O(24)–C(24)–C(25)	120.0(15)
O(14)–C(14)–N(13)	118.2(13)	O(24)–C(24)–N(23)	120.9(14)
C(14)–C(15)–C(16)	118.5(14)	C(24)–C(25)–C(26)	121.0(15)
C(16)–C(15)–C(151)	121.5(14)	C(26)–C(25)–C(251)	121.4(15)
C(14)–C(15)–C(151)	120.0(14)	C(24)–C(25)–C(251)	117.7(15)
C(15)–C(16)–N(11)	120.7(14)	C(25)–C(26)–N(21)	120.8(15)
C(16)–N(11)–C(12)	122.5(13)	C(26)–N(21)–C(22)	118.4(14)
C(11)–N(11)–C(16)	121.7(13)	C(21)–N(21)–C(26)	119.9(14)
C(11)–N(11)–C(12)	115.7(13)	C(21)–N(21)–C(22)	121.6(14)
N(11)–C(12)–N(13)	117.4(13)	N(21)–C(22)–N(23)	118.8(14)
O(12)–C(12)–N(11)	122.0(14)	O(22)–C(22)–N(21)	121.7(15)
O(12)–C(12)–N(13)	120.6(14)	O(22)–C(22)–N(23)	119.4(14)
Angles			
C(32)–N(33)–C(34)	121.5(13)	C(42)–N(43)–C(44)	123.2(13)
Pt(2)–N(33)–C(32)	115.6(10)	Pt(2)–N(43)–C(42)	117.2(10)
Pt(2)–N(33)–C(34)	122.8(9)	Pt(2)–N(43)–C(44)	119.5(10)
N(33)–C(34)–C(35)	122.1(13)	N(43)–C(44)–C(45)	116.3(15)
O(34)–C(34)–C(35)	119.3(13)	O(44)–C(44)–C(45)	125.0(16)
O(34)–C(34)–N(33)	118.5(13)	O(44)–C(44)–N(43)	118.6(15)
C(34)–C(35)–C(36)	116.3(14)	C(44)–C(45)–C(46)	124.4(15)
C(36)–C(35)–C(351)	121.3(14)	C(46)–C(45)–C(451)	118.8(14)
C(34)–C(35)–C(351)	122.3(14)	C(44)–C(45)–C(451)	116.6(14)
C(35)–C(36)–N(31)	122.5(15)	C(45)–C(46)–N(41)	119.6(15)
C(36)–N(31)–C(32)	120.6(14)	C(46)–N(41)–C(42)	121.7(14)
C(31)–N(31)–C(36)	123.8(14)	C(41)–N(41)–C(46)	123.2(14)
C(31)–N(31)–C(32)	115.6(14)	C(41)–N(41)–C(42)	115.1(13)
N(31)–C(32)–N(33)	116.4(14)	N(41)–C(42)–N(43)	114.7(13)
O(32)–C(32)–N(31)	122.2(16)	O(42)–C(42)–N(41)	122.2(14)
O(32)–C(32)–N(33)	121.4(15)	O(42)–C(42)–N(43)	123.0(14)

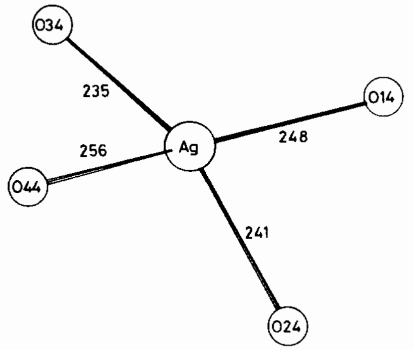

Fig. 3. Coordination of Ag in the title compound. Distances in pm.

donors [16–18] or oxygen donors of amino acids [17] with bond lengths in the order of 2.2 Å.

Distances between the two Pt atoms and Ag are 2.849(1) and 2.884(1) Å, respectively. Quite clearly, they are too long to implicate any strong metal–metal bonding between platinum and silver. However, some weak metal–metal interaction appears feasible on the basis of Pt and Ag radii [19]. Interatomic distances and bond angles of the 1-methylthymine ligands are given in Table III. As can be seen, there are, with the exception of ring 3, no significant differences between corresponding bond lengths of free 1-methylthymine [20] and the 1-methylthyminato ligands in our compound. In ring 3 the C(34)–O(34) bond (1.296(17) Å) is significantly longer than the C(32)–O(32) bond (1.219(21) Å). For ring 1 a similar tendency of C(14)–O(14) lengthening (1.285(19) Å) compared to C(12)–O(12) (1.222(17) Å) is observed, but the differences are close to the limit of significance. In contrast, C–O bond lengths are very similar in rings 2 and 4. The observed 1.296 Å bond length for C(34)–O(34) is similar to that observed in a platinum uracil complex (1.291(15) Å) with an extremely strong hydrogen bond between O(4) and $H_5O_2^+$ unit [21]. It is approaching the lower limit of C–O single bond distances in hydroxo-pyridines which have bond lengths in the order of 1.33–1.35 Å [22]. With O(34) being the oxygen atom closest to the silver atom, it is logical to attribute the C–O lengthening to its influence. The same effect – lengthening of C(4)–O(4) compared to C(2)–O(2) – is also observed in one of the two 1-methylthymine ligands in the already mentioned head-to-tail platinum dimer (1.29(1) Å for C(4)–O(4) and 1.20(2) Å for C(2)–O(2)) [9]. In the corresponding head-to-head dimer [7] the standard deviations are such that no statements concerning significant differences between the coordinating and the non-coordinating keto groups can be made.

There are a few differences in respective bond angles in the four 1-methylthymine rings. However, no clear tendency that could possibly be correlated with the Ag–O distance to the corresponding ring can be seen.

All four 1-methylthymine ligands are roughly planar. Deviations of ring atoms from least-squares planes are ⩽0.03 Å for ring 1, ⩽0.06 Å for ring 2, ⩽0.05 Å for ring 3 and ⩽0.02 Å for ring 4. There are, however, considerable deviations of the two platinum atoms from the ligand planes: Pt(1) lies 0.25 Å outside the best plane through ring 1 and 0.10 Å outside of ring 2, Pt(2) 0.33 Å and 0.15 Å outside ring 3 and 4, respectively. This finding holds up if the positions of the Pt atoms relative to the best planes through C(2), N(3) and C(4) of each ring are calculated, although deviations of the platinum atoms are slightly smaller.

The unit cell contains two nonequivalent sets of nitrates, each one being occupied by one half of the anions. It also contains six sets of H_2O molecules with two sets having a 50% occupancy only (O(5), O(6)). Nitrates and water molecules sitting on partially occupied positions are connected through hydrogen bonds. One nitrate has all three oxygen atoms within 3.2 Å of a water molecule thus accomplishing hydrogen bonding. The second nitrate has only one oxygen strongly hydrogen bonded (2.319(60) Å to $H_2O(6)$ and 2.925(44) Å to $H_2O(4)$), whereas the other two nitrate oxygens are not hydrogen bonded at all. An examination of other relevant hydrogen bonding distances and angles gives the following picture: $H_2O(1)$ is hydrogen bonded to the $NH_3(1)$ group, to $H_2O(3)$ and $H_2O(4)$. At the same time $H_2O(4)$ forms hydrogen bonds with the keto oxygen O(42) of the 1-methylthymine ring 4. $H_2O(2)$ is hydrogen bonded to $NH_3(4)$. $H_2O(6)$ is binding to every second keto oxygen O(22) of ring 2.

*Bis(μ-1-methylthyminato)*cis*-diammineplatinum(II)-Silver Nitrate*

The X-ray structure of the Pt/Ag = 1:1 compound has not been performed. From the way of preparation it can be concluded, however, that platinum is binding through N(3) of the 1-methylthymine ligands as well. From IR spectra (*vide infra*) it is evident, that the interaction between Ag and 1-methylthymine must be essentially ionic and similar to that occurring in the Pt/Ag = 2:1 compound. Several structures appear feasible: a monomeric structure with Ag binding to two exocyclic oxygens of 1-methylthymine ligands and to two other atoms (oxygens of water of crystallization or nitrate) or a di- or polymeric structure with Ag bridging oxygen atoms of 1-methylthymine ligands of different bis(1-methylthyminato-N3)*cis*-diammineplatinum(II) units.

Infrared Spectra

Neutral 1-methylthymine, likewise thymine, thymidine, uracil and uridine, are poor ligands for

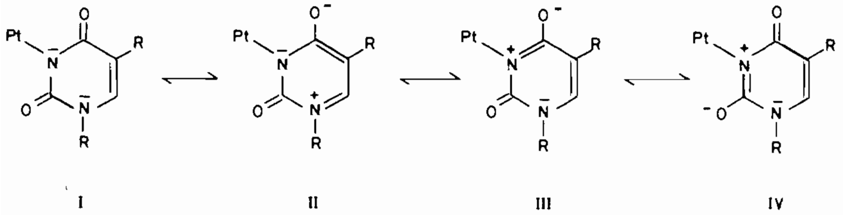

Fig. 4. Proposed resonance structures of the 1-methylthyminato ligand upon platination at N(3). R = CH_3.

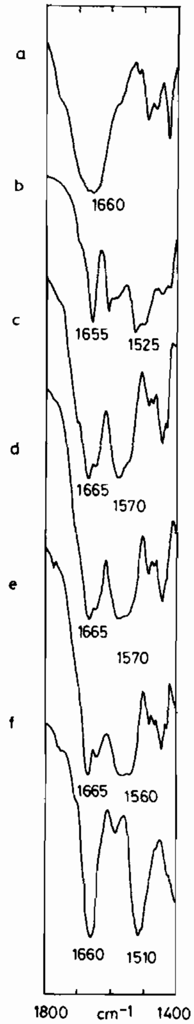

Fig. 5. Infrared spectra between 1800 and 1400 cm^{-1} of (a) 1-methylthymine, (b) potassium 1-methylthyminate, (c) bis-(1-methylthyminato)*cis*-diammineplatinum(II), (d) the Pt/Ag = 2:1 complex, (e) the Pt/Ag = 1:1 complex, and (f) bis(μ-1-methylthyminato-N3, O4)bis(*cis*-diammineplatinum(II))dinitrate (head-to-head).

platinum. Only a very limited number of metal complexes of these ligands in their neutral forms have been reported so far, but there is no platinum complex among these [23]. It has long been assumed that there is no complex formation between platinum and pyrimidine-2.4 diones at all. However, once N(3) is deprotonated, or N(1) with unsubstituted pyrimidine-2.4 diones [24], the anion is acting as a good ligand for platinum with formation of a number of complexes [25].

We now find that N(3) platinated 1-methylthymine ligands also act as good complex forming agents. Binding has thus far been established for platinum [7] and now for silver. In the case of silver the interaction is essentially ionic, with *cis*-diammineplatinum(II) [7] it is covalent. The effects of N(3) platinum binding on the 1-methylthymine ring and further binding of a metal cation to the exocyclic oxygen O(4) can be studied in the double bond stretching region of the infrared spectra. In Fig. 4 the IR spectra of 1-methylthymine, its anion and several Pt and Pt/Ag complexes in the region 1800–1400 cm^{-1} are given. In the spectrum of neutral 1-methylthymine a broad band centered around 1660 cm^{-1} is observed which is due to C = C and C = O stretching modes, most likely coupled as usual in similar heterocyclic systems. Upon deprotonation, the double bond stretching region is strongly affected as a consequence of the delocalization of π electrons in the heterocyclic ring and the exocyclic groups. A splitting of the original broad single band is observed and a shift to lower frequency of one strong component. The new intense band around 1500 cm^{-1} in the spectrum of the anion is assigned to a vibration of the O···C···N···C···O moiety with the dominant contribution of the C···O groups [26].

In the bis(1-methylthyminato-N3)*cis*-diammineplatinum(II) compound the band pattern in the 1800–1400 cm^{-1} range still resembles the anion much more than the neutral species. Thus the effect of platinum on the electronic distribution in the 1-methylthymine ring is not nearly as strong as that of the proton. As a consequence, the exocyclic keto groups – or at least C(4)O – are (is) sufficiently basic to accomplish additional binding of a metal. Therefore resonance structures of type II and III shown in Fig. 5 may be considered to contribute strongly to the actual charge distribution in the ring and be responsible for the good ligand properties of N(3) platinated 1-methylthymine rings. Binding of silver to the C(4)O group appears to stabilize a geometry with substantial contributions of resonance structures with sp^3 hybridization at N(3). This leads to a significant movement of platinum out of the ligand plane.

With the second cation binding in an ionic fashion to the N(3) platinated ligand, the infrared spectrum of the parent compound remains essentially unchanged (*cf.* Figs. 5c, 5d and 5e) [27]. With covalent binding of a second metal to one of the exocyclic oxygens, as with the head-to-head dimer bis(μ-1-methylthyminato-N3,O4)bis(*cis*-diammineplatinum(II)) dinitrate [7], the double bond character of the coordinating keto group is further reduced and the corresponding vibration shifted to lower energy (Fig. 5f). The now established property of N(3) platinated 1-methylthymine to bind other cations may explain why reaction between *cis*-$Pt(NH_3)_2^{2+}$ and 1-methylthymine as well as related ligands leads to compounds with presumably oligomeric structures [28]. The structures of these so called 'platinum pyrimidine blues' are of interest since they represent potentially powerful antitumor agents [29].

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